Eurotransplant Senior DR-compatible Program

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Reduce acute rejection rates in the Old-for-Old kidney transplantation program. Less acute rejection in these vulnerable older kidneys inevitable translates in better initial kidney function. Less need for acute rejection treatments with high dose...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON38038

Source
ToetsingOnline

Brief title
ESDP

Condition

- Other condition

Synonym
kidney transplantation, renal replacement therapy

Health condition

niertransplantatie

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Astellas Pharma,Hoffmann-La Roche,Investigator-driven studie;subsidie voor aanpassing allocatie algorithmen en data acquisitie door bedrijven

Intervention

Keyword: Elderly, HLA-DR matching, Kidney transplantation, Old-for-Old allocation

Outcome measures

Primary outcome

The primary comparison will involve an *intention-to-treat* analysis of

• Incidence of biopsy-proven acute rejection (BPAR) 6 months

post-transplantation

• Incidence of steroid-resistant and recurrent acute rejection (requiring

antibody therapy)

Secondary outcome

All secondary assessments will be conducted amongst the entire study

population, and will be of the effects of initial allocation (with or without

matching for HLA-DR) on safety outcomes and efficacy measures:

•Primary non function (PNF); delayed graft function (DGF, defined by dialysis

requirement within 7 days post transplant or spontaneous decrease of serum

creatinine >10% per day for 3 consecutive days occurring beyond the seventh day

post transplant)

•Graft function at month 3, 6, 12 and yearly up to 5 years (calculated GFR,

using the Modified Diet in Renal Disease [MDRD] equation).

•Incidence of Late Acute rejection (BPAR occurring between month 6 and 12);

•Presence of donor specific antibodies (DSA) at 6 months (ETRL), these sera will also be used to calibrate for differences in the creatinine assays.

•Graft survival (including cause of graft loss);

•Patient survival (including cause of death);

•Incidence of cardiovascular events (sudden death, PTCA, CABG, non-fatal acute myocardial infarction, CVA, peripheral vascular disease);

•Incidence of infections (sub-classified as mild, serious and life threatening);

•Incidence of malignancy (including post-transplantation lymphoproliferative disorder);

•Incidence of anaemia, leukopenia, thrombocytopenia as well as comparison of median values of haemoglobin, white cell count and platelet count);

•Blood pressure (assessed by readings at clinic visits, use of antihypertensive medication);

•Number of days in hospital during index admission and total in the first year, excluding admission or scheduled surgery for non-transplant related medical issues;

•Subset analyses based on waiting-time; cold ischemia time; HLA-DR compatibility; donor and/or recipient age >= 70 years.

Study description

Background summary

The current *Eurotransplant Senior Program* allocates kidneys from older donors(at least 65 year), without prospective matching for HLA antigens, to older (at least 65 years) local transplant candidates (13). The ESP program was introduced in 1999 and has resulted in a significant increase in availability

of kideney older donors for transplantation and consequentely more elderly dialysis patients have placed on the kidney waiting list. Besides these advantages, several studies have documented higher acute rejection rates in recipients of kideney fron older donors, independent of the age category of the recipients. It is conceivable that prophylactic treatment with anti-lymphocyte antibodies attenuates the interaction between renal aging changes, ischemia-reperfusion injury and the ensuing immune response. Thus, at least theoretically, it should be possible to improve the outcome of older donor kidneys in young recipients by providing more intensive immune suppression in the early post-operative period in order to prevent excess rejection rates. Such an approach may be acceptable for younger recipients, but remains to be determined for the elderly. The therapeutic index for clinical immune suppression appears to be even narrower in the elderly than in younger renal transplant recipients.
In the elderly, cardiovascular and especially infectious causes are among the leading primary causes of death. There is no doubt that extra boluses of steroids, recycling of the steroid taper or treatment with poly- or monoclonal antibodies add significantly to post-transplant morbidity and mortality.
We propose that introduction of prospective matching for HLA-DR antigens in the context of Old-for-Old allocation may result in less acute rejection episodes, better preservation of renal function as well as less infectious cause morbidity and mortality.

Study objective

Reduce acute rejection rates in the Old-for-Old kidney transplantation program. Less acute rejection in these vulnerable older kidneys inevitable translates in better initial kidney function. Less need for acute rejection treatments with high dose intravenous steroids and/or polyclonal anti T-cell antibodies will allso reduce to incidence of inctious cause mortality, the leading cause of death in the elderly transplant recipient.

Study design

Observational, prospective, randomized multicenter allocation study to compare the impact of prospective matching for HLA-DR antigens between donor and recipient on outcome parameters in the Eurotransplant Senior Program (ESP). Paired kidneys from 300 donors >= 65 year of age will be randomized at the center or (cooperating) regional level: the first kidney according to current ESP allocation (waiting time, no prospective matching for HLA antigens) and the contra-lateral kidney aimed at zero mismatches for HLA-DR followed by waiting time. Cold ischemia times should be as short as possible, but always under 20 hours.
In the participating centers recipients will be treated with an evidence-based standardized immunosuppressive regimen. This regimen is already standard therapy in the large majority of transplant centers and its superior efficacy

has been documented in the largest prospective study in de novo trenal transplant recipients to date.

Study burden and risks

This is an observational allocation study and there is no additional burden associated with participation. The proposed HLA matching will, according to all medical knowledge, not negatively but rather positively influence the outcome of the selected patients. Treatment regimens and outpatient department visits are according to (evidence-based) standard medical care for renal transplant recipients and their follow-up. The amount and number of blood samples, physical examinations or other tests are the same in both groups and according to current standard care after renal transplantation.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients > 64 years of age
Placed on the Eurotransplant Kidney Waiting List

Exclusion criteria

• Active systemic infection;
• HIV (antigen or antibody), hepatitis B (HBsAg), or hepatitis C (antibody) positivity;
• History of malignancy within five years of enrolment (with the exception of adequately treated non-melanoma skin cancer);
• Known to be poorly compliant with clinic visits or prescribed medication;
• Medical history that might limit the individual*s ability to take the defined immunosuppressive agents.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-01-2010
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	24-02-2009
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	16-04-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	28-08-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	20-11-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	19-12-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL24085.058.08